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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/006,957 | 12/04/2001 | Shoshana Paglin | AP33710 072734.0121 | 2771 |

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BAKER & BOTTS
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NEW YORK, NY 10112

EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT PAPER NUMBER

1623

DATE MAILED: 09/23/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary

Application No.

10/006,957

Applicant(s)

PAGLIN ET AL.

Examiner

Traviss C McIntosh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 22-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

The Amendment filed June 30, 2003 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 3, 10, 15, 17 and 21 have been amended.

Remarks drawn to rejections of Office Action mailed March 26, 2003 include:

Claim objections: which have been overcome by applicants' amendments and have been withdrawn.

112 2nd paragraph rejections: which have been overcome by applicants' amendments and have been withdrawn.

103(a) rejections: which have been withdrawn in part and maintained in part.

Claims 22-32 are withdrawn from further consideration. These claims are drawn to a non-elected invention without traverse as set forth in paper #5.

An action on the merits of claims 1-21 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite wherein the claim is drawn to a “modulator” of vacuolar proton ATPase activity. It is unclear as to what is intended by a “modulator”, as this could represent a compound that increases the ATPase activity, or decreases the ATPase activity. Clarity is respectfully requested.

Claims 1 and 13 are confusing wherein the claims read: “a method for promoting cell death following exposure to a cytotoxic agent comprising...”. This phrase would be more favorably considered as “a method of promoting cell death in a cell which has previously been exposed to a cytotoxic agent comprising...” to clearly articulate in the preamble that it is the cell which has been previously treated with a cytotoxic agent, and that this is also the cell which the method is to be practiced on.

Likewise, claims 3 and 15 would be more favorably considered as “a method of promoting cell death in a cell which has previously been exposed to irradiation comprising...”.

All claims which depend from an indefinite claim are also indefinite. Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-8, 11-14, and 16-19 rejected under 35 U.S.C. 102(b) as being anticipated by Altan et al. (Document 18 of IDS submitted 2/10/2003).

The claims the instant application are drawn to the following: claim 1 is drawn to a method of promoting cell death following exposure to a cytotoxic agent comprising contacting said cell with a modulator of vacuolar proton ATPase activity. Claim 13 is drawn to a method for promoting cell death following exposure to a cytotoxic agent comprising contacting said cell with an agent capable of inhibiting acidic vesicular function or acidification. Dependent claims 2 and 14 limit the cells of claims 1 and 12 to cancer cells. Dependent claims 4 and 16 limit the cytotoxic agent to a chemotherapeutic agent. Dependent claim 5 limits the modulator to an inhibitor of vacuolar proton ATPase activity. Dependent claim 6 limits the inhibitor to a macrolide antibiotic. Dependent claim 7 limits the macrolide to bafilomycin A1. Dependent claim 8 limits the inhibitor to concanamycin.

Altan et al. disclose that administering monensin, bafilomycin A1, or concanamycin to a cell which is resistant to adriamycin from previous therapies, sufficiently changes the cells to that of a drug-sensitive cell thereby rendering the cell vulnerable once again to chemotherapy. Thus, Altan teaches to administer the claimed compounds, which are known in the art to be inhibitors of V-ATPase activity, which is known in the art to promote proton conduction across the vesicle membrane thus inhibit acidification of vesicles, to cells which have been previously treated with a cytotoxic agent (adriamycin, a known chemotherapeutic agent), thereby promoting cell death by once again rendering them vulnerable to chemotherapy (abstract).

Claim Rejections - 35 USC § 103

Claims 9, 10, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altan et al., as set forth supra, in view of Boyd et al. (reference 1 the IDS submitted 2/10/2003).

Claims 9 and 20 of the instant application limit the modulator/inhibitor of claims 5 and 13 to a benzolactone enamide, and claims 10 and 21 limit the benzolactone to salicylhalamide A. (Additionally, as noted in the Office Action dated 3/26/2003, these claims do not receive the priority date of 12/4/2000, but receive a date of 12/4/2001).

Altan et al. teach the method of administering monensin, bafilomycin A1, or concanamycin to a cell which is resistant to adriamycin from previous therapies, sufficiently changes the cells to that of a drug-sensitive cell thereby rendering the cell vulnerable once again to chemotherapy. What is not taught is to administer to a benzolactone enamide or salicylhalamide A.

Boyd et al. teach that benzolactone enamides, including salicylhalamide A, are inhibitors of the growth of tumor cells as they inhibit vacuolar proton ATPase activity.

It would have been obvious to one of ordinary skill in the art to administer a compound which has an art recognized activity (inhibit vacuolar proton ATPase activity) for another compound which has the same art recognized activity in a correlative method. Likewise, one of ordinary skill in the art would have a reasonable expectation of success in practicing the method of Altan et al. with the vacuolar proton ATPase inhibitors of Boyd et al. as both compounds are known in the art to have the same effects vacuolar proton ATPase activity. One would be motivated to use the compounds of Boyd et al. in the method of Altan et al. because Altan et al.

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teaches that inhibitors of vacuolar proton ATPase activity (bafilomycin A1) are effective in resensitizing cells to chemotherapeutic agents after they have been previously treated unsuccessfully with a chemotherapeutic agent, and Boyd et al. teaches that the benzolactone enamides, including salicylhalamide A, are inhibitors of the growth of tumor cells as they inhibit vacuolar proton ATPase activity.

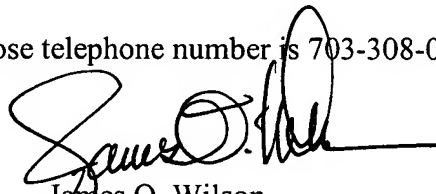
Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh III
September 12, 2003